

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/549,804	RUSSELL ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	STEVEN C. POHNERT	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 10 October 2008.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 20-25 and 29-46 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 20-25 and 29-46 is/are rejected.  
 7) Claim(s) 21 is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on 19 September 2005 is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input checked="" type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. <u>8/28/2009</u> .                          |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application  |
| Paper No(s)/Mail Date <u>1/24/2006, 9/19/2005</u> .                                    | 6) <input type="checkbox"/> Other: _____.                          |

**DETAILED ACTION**

***Election/Restrictions***

1. Applicant's election with traverse of Group 2, claims 20-46 in the reply filed on 5/14/2008 is acknowledged. The traversal is on the ground(s) that the response asserts the Sambrook reference does not teach the value of the SNPs as a prognostic indicator in inflammatory conditions. This is not found persuasive because the claims are drawn to compositions and as presented require an oligonucleotide or restriction enzymes.

The teachings of Sambrook meet the structural limitations of the claims.

In view of the amendment of 10/10/2008 claim 20 to require either a polymorphic site at position 12580 of SEQ ID NO 1 or a site in linkage disequilibrium therewith the further restriction is withdrawn.

Claims 20-25 and 29-46 are pending and being examined.

***Priority***

The instant application was filed on 3/29/2006 as a National Stage entry of PCT/CA04/00424 filed 3/19/2003 which claims priority to US Provisional 60/4555,550 filed 3/19/2003.

***Specification***

2. The disclosure is objected to because of the following informalities:
3. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. The specification contains a hyperlink on page 39, line 16. Applicant should inspect the rest of the application to Applicant is required

to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

***Claim Objections***

4. Claim 21 is objected to because of the following informalities: The claims is drawn to polymorphic sites in linkage disequilibrium with position 12580 then recites that 12580 is one of the positions. The claim should be amended so that it no longer recites 12580 as a position that is in linkage disequilibrium with itself. Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 20, 22-25 and 29-35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejected claims 20, 22-25 and 29-35 are drawn to a kit for determining the genotype of a subject at a polymorphic site at nucleotide position 12580 of SEQ ID NO:1 or a site in linkage disequilibrium therewith, which genotype is prognostic of the subjects ability to recover from an inflammatory conditions

When the claims are analyzed in light of the specification, the invention encompasses an enormous number of nucleotide molecules. The specification teaches that polymorphic sites 5645, 7121, 7437, 8070, 8406, 9463, 9466, 12219, 13889 and 14440 are in linkage disequilibrium with position.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been by full structure. The instant specification teaches 10 nucleic acid sequences. The presence of claim 21 clearly indicates that the polymorphisms in linkage disequilibrium with position 12580 of SEQ ID NO 1 is broader than those specifically recited. It encompasses any polymorphism that is at any level of linkage disequilibrium and thus encompasses every nucleotide in the genome.

Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (e.g. other nucleotide sequences or positions within a specific gene or nucleic acid), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case the specification provides no structural limitations to identify polymorphic sites in linkage disequilibrium with position 12580 of SEQ ID NO 1, other than the polymorphisms specifically disclosed 5645, 7121, 7437, 8070, 8406, 9463, 9466, 12219, 13889 and 14440. The claims read in light of the specification encompass any nucleic acid molecule that can broadly be interpreted as in any level of linkage disequilibrium with position 12580 of SEQ ID NO 1. This broadly encompasses every

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nucleotide in the genome as all nucleotides in the genome are in some level of linkage disequilibrium with every other nucleotide in the genome.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polymorphisms in linkage disequilibrium with position 12580 of SEQ ID NO 1regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. The current situation is a definition of the compound solely based on its functional utility, polymorphisms in linkage disequilibrium with position 12580 of SEQ ID NO 1regardless, without any definition of the particular polymorphisms claimed.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus,

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an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

In the instant application, the provided information regarding nucleic acid polymorphisms in linkage disequilibrium with position 12580 of SEQ ID NO 1 regardless, do not constitute an adequate written description of the broad subject matter of the claims, and so one of skill in the art cannot envision the detailed chemical structure of the nucleic acids encompassed polymorphisms in linkage disequilibrium with position 12580 of SEQ ID NO 1. Adequate written description requires more than a statement that nucleic acids with a particular quality are part of the invention and reference to a potential method for their identification. The nucleic acid sequence is required.

In conclusion, the limited information provided regarding polymorphisms in linkage disequilibrium with position 12580 of SEQ ID NO 1 is not deemed sufficient to reasonably convey to one skilled in the art nucleic acid molecules claimed.

Thus, having considered the breadth of the claims and the provisions of the specification, it is concluded that the specification does not provide adequate written description for the claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claims 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 33 and 34 recites the limitation "the technique" in the first line. There is insufficient antecedent basis for this limitation in the claim as "the technique" is not previously recited in claim 30 or claim 20 which it depends. This rejection can easily be overcome by amending the claim to depend from claim 32.

10. Claim 35 recites the limitation "the determining" in the first line. There is insufficient antecedent basis for this limitation in the claim as "the determining" is not previously recited in claim 30 or claim 20 which it depends. This rejection can easily be overcome by amending the claim to depend from claim 32.

#### ***Claim Rejections - 35 USC § 102***

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 20, 23, 24, 25, 30, 32, 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Henry et al (Arteriosclerosis, Thrombosis and Vascular Biology (1998) volume 19, pages 84-91).

As noted in the MPEP 2111.02, "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition

of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." Accordingly, the claim language of "a kit useful for determining a genotype of a subject or subjects at a polymorphic site at nucleotide position 12580 of SEQ ID NO 1" merely sets forth the intended use or purpose of the claimed kit, but does not limit the scope of the claims other than setting forth position 12580 of SEQ ID NO 1.

Although claim 20, 23, 24, 25, 30, 32, 33 recites the term "kit", the claim contains no structural requirements to distinguish it from a composition, nor is the term defined to be so limited in the specification. Accordingly, the claim has been given the reasonable interpretation to encompass a composition containing the claimed molecule.

With regard to claim 20, 23, 24, 25, 30, 32, 33, the limitation that the kits contain instructions, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. See *In re Ngai*, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004)(holding that an inventor could not patent known kits by simply attaching new set of instructions to that product).

Henry teaches that PCR amplification followed by restriction enzyme cleavage was performed to detect polymorphisms in PAI-1 (page 85, 2<sup>nd</sup> column). Henry thus teaches a kit for detection a polymorphisms in linkage disequilibrium with position 12580 of SEQ ID NO 1 by use of primers and a restriction enzyme.

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

15. Claims 20, 30, 34, 36, 37 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Menges et al (Lancet (2001) volume 357, pages 1096-1097) in view XU et al (WO01/81631 published 1/11/2001) (IDS 1/24/2006) and GenBank Accession AF386492.2 GI:14488407 (June 19, 2001).

As noted in the MPEP 2111.02, "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." Accordingly, the claim language of "a kit useful for determining a genotype of a subject or subjects at a

polymorphic site at nucleotide position 12580 of SEQ ID NO 1" merely sets forth the intended use or purpose of the claimed kit, but does not limit the scope of the claims other than setting forth position 12580 of SEQ ID NO 1.

Although claim 20, 30, 34, 36, 37 and 39 recites the term "kit", the claim contains no structural requirements to distinguish it from a composition, nor is the term defined to be so limited in the specification. Accordingly, the claim has been given the reasonable interpretation to encompass a composition containing the claimed molecule.

With regard to claim 20, 30, 34, 36, 37 and 39, the limitation that the kits contain instructions, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. See *In re Ngai*, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004)(holding that an inventor could not patent known kits by simply attaching new set of instructions to that product).

Menges teaches that the PAI promoter polymorphism 4G/5G is thought to play a role in prognosis from severe trauma. Menges teaches that subjects with the 4G/4G genotype were more likely to have sepsis and multiorgan failure than subjects with the 5G/5G genotype (table). Menges teaches genomic DNA was isolated.

Menges does not teach a kit using a proof reading polymerase (claims 34 and 39).

However, Xu et al a method and kit useful for detection and identifying nucleic acid variants in a nucleic acid (page 2). Xu teaches his method overcome the

shortcomings of the prior art including, cost, relative long analysis times, use of radiolabeled reagents, complexity and/or being poorly suited for multiplex analysis.

GenBank Accession AF386492.2 GI:14488407 (June 19, 2001) teaches the sequence of instant SEQ ID NO 1, including the 4G/5G site.

Therefore it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was have oligonucleotides and proofreading polymerases in a kit as taught by Xu to analyze mutation in the PAI-1 gene in linkage disequilibrium with position 12580 of SEQ ID NO 1. The artisan would have a reasonable expectation of success as the artisan is merely using known methods to detect known mutations.

16. Claims 20-22, 25, 29-33, 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henry et al (Arteriosclerosis, Thrombosis and Vascular Biology (1998) volume 19, pages 84-91) in view GenBank Accession AF386492.2 GI:14488407 (June 19, 2001) and Chee et al (WO 95/11995).

As noted in the MPEP 2111.02, "If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention's limitations, then the preamble is not considered a limitation and is of no significance to claim construction." Accordingly, the claim language of "a kit useful for determining a genotype of a subject or subjects at a polymorphic site at nucleotide position 12580 of SEQ ID NO 1" merely sets forth the intended use or purpose of the claimed kit, but does not limit the scope of the claims other than setting forth position 12580 of SEQ ID NO 1.

Although claim 20-22, 25, 29-33, 35 recites the term “kit”, the claim contains no structural requirements to distinguish it from a composition, nor is the term defined to be so limited in the specification. Accordingly, the claim has been given the reasonable interpretation to encompass a composition containing the claimed molecule.

With regard to claim 25, 29, 42, 45-46, the limitation that the kits contain instructions, the inclusion of instructions is not considered to provide a patentable limitation on the claims because the instructions merely represent a statement of intended use in the form of instructions in a kit. See *In re Ngai*, 367 F.3d 1336, 70 U.S.P.Q.2d 1862 (Fed. Cir. 2004)(holding that an inventor could not patent known kits by simply attaching new set of instructions to that product).

With regards to claim 41, the courts have held that “while features of an apparatus may be recited either structurally or functionally, claims directed to an apparatus must be distinguished from the prior art in terms of structure rather than function.” *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). In addition, “[A]pparatus claims cover what a device *is*, not what a device *does*.” *Hewlett-Packard Co. v. Bausch & Lomb Inc.*, 909 F.2d 1464, 1469, 15 USPQ2d 1525, 1528 (Fed. Cir. 1990) (emphasis in original). Thus teaching of the structural elements of the kit renders the instant claims obvious.

Henry teaches PAI-1 has been implicated in insulin resistance, coronary heart disease and inflammatory status (84, 1st column). Henry teaches there is accumulating evidence that genetic control plays a role in circulating PIA-1 levels and 8 polymorphism have been identified (84, 2nd column).

Henry does not teach detection of a polymorphic site of 12219 or 12580. Henry does not teach oligonucleotides selected from SEQ ID NO 2-SEQ ID NO 11. Henry does not teach sequencing.

However, Chee et al (WO 95/11995) teaches an array of capture probes (see figure 16, and page 79 lines 23-39) and block tiling arrays (see Figure 7 and page 37 line 10- page 38 line 34). Chee teaches the use of immobilized arrays to interrogate a reference sequence and its codons with a target sequence for the identification of single base mutants possible in the reference sequence can associated with disease (see page 31 lines 6-7, and page 11 line 9 and 10). Further Chee teaches this approach allows simultaneous detection and quantification of multiple target sequences (see page 32 lines 18-19), allowing for sequence determination. The block-tiling array allows the interrogation of multiple nucleotide sites by use of multiple probe sets, which represent every permutation of nucleotides possible for a give sequence. Chee teaches a method of mutation detection for analyzing known target sequences for individual mutant sites and immediately adjacent bases (see page 18, lines 1-8). The tiling arrays of Chee result in sequencing by hybridization of the entire sequence of interest. Chee teaches the determination of all possible combinations of nucleotides surrounding a SNP, allowing determination of all possible nucleic acid. Chee teaches the use of capture probes of 15 to 30 nucleotides, perfectly complementary to the DNA of interrogation (see page 27 lines 2-6).

Therefore it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to examine the PAI-1 sequence taught by

GenBank Accession AF386492.2 GI:14488407 in the method of Chee. The artisan would be motivated to determine identify additional mutations in the PAI-1 that could account for the alterations in PAI-1 activity associated alter PAI-1 levels including diabetes, inflammation and sepsis as Taught by Henry. The tiling array of Chee as applied to the known PAI-1 sequence taught would result in a kit containing a microarray with probes that would allow for detection of any polymorphism in the sequence by a tiling sequencing array thus rendering the instant claims obvious.

### **Summary**

No claims are allowed.

### **Conclusions**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STEVEN C. POHNERT whose telephone number is (571)272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, every second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Steven C Pohnert/  
Examiner, Art Unit 1634  
Steven Pohnert